REMARKS

The above-identified patent application has been amended and Applicants respectfully request the Examiner to reconsider and again examine the claims as amended in accordance with the provisions of 37 C.F.R §1.116.

Claims 1-41 and 44-51 are pending in the application. No claims are allowed. Claims 1-41 and 44-49 are rejected. Claims 1, 6, 7, 21, 26, 28, 47, and 49 are amended herein. Claims 3, 5, 23, 25, 40, 47, and 49 are also amended herein, but not for reasons of patentability, as will be apparent. Claims 46 and 48 are canceled herein without prejudice. Claims 50 and 51 are new.

Regarding the Response to Arguments

The Examiner asserts that "[t]he applicant clearly defines, on page 8 of the instant specification, a "visible wavelength range of about 400 nm to 700 nm and an 'NIR range of 700 nm to 1000 nm.'" Applicants submit that the Examiner has partially incorrectly quoted from the specification.

At paragraph [0044] of the published application, it is recited "the visible wavelength range of about 400nm to 700nm" and "the near infra red (NIR) range of about 700nm to 1000nm."

The Examiner apparently attempts to define a strict boundary between visible and near infrared light, when no strict boundary was stated by the Applicants and when no strict boundary exists, as will be recognized by those of ordinary skill in the art. Further discussion of wavelength is given below.

The Examiner asserts that light with a wavelength of 694 nanometers is visible light. Applicants disagree. Applicants submit that a boundary of visible light is at about 700 nanometers, but not necessarily at 700 nanometers. Applicants also submit that near infrared

light will be understood to be light having a wavelength just beyond that which is visible to the human eye, i.e., not visible. Since human sight varies, Applicants submit that a boundary between visible and near infrared light can be drawn at about 700 nanometers, but not necessarily at 700 nanometers.

The Rejections under 35 U.S.C. §112, Second Paragraph

The Examiner rejects Claims 46 and 48 under 35 U.S.C. §112, second paragraph. The Examiner asserts that "[t]he term 'about' "is not defined in the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention." Applicants respectfully disagree.

The term "about" is used in Claims 46 and 48 in the phrase "the visible wavelength range has a smallest wavelength of about four hundred nanometers." Support for this phrase can be found, for example, in paragraphs [0044] and [0051] of the published application, where it is stated "the visible range of about 400 to 700 nm."

Applicants continue to submit that wavelength boundaries of visible light are notoriously well know to be "about 400 to 700 nanometers" and that these boundaries will be very well understood by those of ordinary skill in the art. As evidence thereof, Applicants attach hereto a first page of a web page at the web site Wikipedia, at http://en.wikipedia.org/wiki/Light, where it is stated that "light is electromagnetic radiation, particularly radiation of a wavelength that is visible to the human eye (**about** 400-700 nm, or perhaps 380-750 nm... ." [emphasis added] Applicants submit that one of ordinary skill in the art will fully understand the approximate wavelength boundaries of visible light and will also fully understand that the wavelength boundaries are not represented by fixed values.

Applicants also respectfully direct the Examiner attention to MPEP 2173.05(b)A. where the term "about" is discussed. According to the MPEP, "[i]n determining the range encompassed by the term "about", one must consider the context of the term as it is used in the specification

and claims of the application." Applicants submit that the phrase "about 400 nanometers" recited in Claims 46 and 48 should be considered in the context of visible light wavelengths. For reasons described above, Applicants further submit that the phrase "about 400 nanometers" is in accordance with common descriptions of the wavelength boundaries of visible light, as will be understood by those of ordinary skill in the art.

In view of the above, Applicants submit that the rejection of Claims 46 and 48 under 35 U.S.C. §112, second paragraph, should be removed.

The Rejections under 35 U.S.C. §102(b)

The Examiner rejects Claims 1-7, 9-11, 13, 19-26, 28-30, 32, 38-39, and 44-49 under 35 U.S.C. §102(b) as being anticipated by Ntziachristos et al. (International Publication number WO 02/041760 A2)

Claim 1 is amended here to incorporate much, but not all of the limitations of Claim 6, and also to incorporate all of the limitations of Claim 7, which depends to Claim 6. In addition, Claim 1 is amended herein to include two new phrases, namely: "visible wavelength range spanning from about 400 nanometers to about 700 nanometers" and "throughout a substantial portion of the visible wavelength range."

Similarly, Claim 21 is amended here to incorporate much, but not all of the limitations of Claim 26, and also to incorporate all of the limitations of Claim 28, which depends to Claim 26. In addition, Claim 21 is amended herein two include two new phrases, namely: "visible wavelength range spanning from about 400 nanometers to about 700 nanometers" and "throughout a substantial portion of the visible wavelength range."

Applicants submit that amended Claims 1 and 21 are patentably distinct over Ntziachristos et al., since the cited reference neither describes nor suggests "... an apparent light

source configured to project excitation light toward a specimen having *fluorescent proteins* therein, ... *the visible wavelength range spanning from about 400 nanometers to about 700 nanometers*...[and] *a diffusion equation having a modified diffusion coefficient selected in accordance with the propagation of visible light in the diffuse medium throughout a substantial portion of the visible wavelength range*," as set forth in Claims 1 and 21.

With this particular arrangement, in some embodiments, the present invention provides the claimed system using **fluorescent proteins that are excited by visible light**. Support for the claimed arrangement can be found, for example, at paragraph [0044] of the published US application where it is stated:

> In some embodiments, the modified diffusion coefficient allows the model to predict light propagation for light in the visible wavelength region, having a wavelength of about 400 nm to 700nm. In other embodiments, the modified diffusion coefficient allows the model to predict light propagation for light in the near infrared wavelength region, having a wavelength of about 700 nm to 1000nm. In still other embodiments, the modified diffusion coefficient allows the model to predict light propagation for light having a wavelength outside of the range of 400nm-1000nm.

As Applicants have stated above, it should be recognized that wavelength boundaries of visible light and of near infrared light are not precisely defined in general. Nevertheless, it should be clear from the written description of the present patent application that the system and methods described therein are targeted at least at the visible region of the spectrum of light.

A system suitable for optical tomography at visible wavelengths of light will be understood to be difficult to achieve. For example, at page 3 of the corresponding published PCT application, it is stated:

> As is known, all currently available fluorescent proteins utilize excitation light having a wavelength in the visible range. Moreover, conventional fluorescent proteins emit visible fluorescent light when excited. Tomographic imaging using visible light, as provided by the conventional fluorescent proteins, is complicated by a relatively high absorption of visible light propagating in biological tissue, which results in significant attenuation. With high absorption,

> (e.g., for visible light) the conventional diffusion approximation described above is not valid.

Using visible light has particular advantages not achieved when using light having longer wavelengths. For example, in paragraph [135] of the published US application, it is stated:

> It should be appreciated that the method and system of the present invention, when using visible light, provides higher spatial resolution than conventional tomographic approaches using near-infrared (NIR) light.

In contrast, Ntziachristos et al. provides a system that operates **using near infrared (NIR) light** (see, e.g., abstract). Ntziachristos et al. describes optical tomography using a variety of fluorescent probes, **which are not fluorescent proteins**, which are recited in Claim 1 and 21. For example, at page 18, Ntziachristos et al. describes a fluorochrome Cy 5.5 with an excitation wavelength of 673 nanometers and an emission wavelength of 694 nanometers. Cy5.5 is described to be a near infrared (NIR) probe.

For example, beginning at page 11, Ntziachristos et al. describes "Activatable NIR Fluorescent Probes," which include Cy5.5 at page 14, which is used by the Examiner as indicative of visible light fluorescent emission. Also, beginning at page 14, Ntziachristos et al. describes "Other NIR Fluorescent Probes. " Applicants submit that Ntziachristos et al. is concerned only with propagation of near infrared light in tissue, which does not present the same difficulties as propagation of visible light outside of the near infrared range in tissue. Thus, Ntiziachristos et al. does not provide the modified diffusion coefficient as claimed.

Arguendo, even if Applicants agreed that the wavelengths described by Ntziachristos et al. are visible wavelengths, and they do not, still, Ntziachristos et al. does not provide the claimed *modified diffusion coefficient selected in accordance with the propagation of visible light in the diffuse medium* ***throughout a substantial portion of the visible wavelength range***.

In view of the above, Applicants submit that independent Claims 1 and 21 are patentably distinct over Ntziachristos et al.

Claims 2-7, 9-11, 13, 19, 20, 44, and 47 depend from and thus include the limitations of Claim 1. Thus, Applicants submit that Claims 2-7, 9-11, 13, 19, 20, 44, 46, and 47 are patentably distinct over the cited reference at least for the reasons discussed above in conjunction with Claim 1. Claims 22-26, 28-30, 32, 38-39, 45, and 49 depend from and thus include the limitations of Claim 21. Thus, Applicants submit that Claims 22-26, 28-30, 32, 38-39, 45, 48, and 49 are patentably distinct over the cited reference at least for the reasons discussed above in conjunction with Claim 21. As described above, Claims 46 and 48 are canceled herein without prejudice.

For reasons discussed above in conjunction with Claims 1 and 21, Applicants submit that Claims 3 and 23 are further patentably distinct over Ntziachristos et al., since the cited reference neither describes nor suggests "... *the fluorescent light has a wavelength in the visible wavelength range and outside of the near infrared range*," as set forth in Claims 3 and 23.

Applicants submit that Claims 4 and 24 are further patentably distinct over Ntziachristos et al., since the cited reference neither describes nor suggests "... *the fluorescent light has a wavelength in a red portion of the visible wavelength range*," as set forth in Claims 4 and 24. The Examiner uses the Cy 5.5 fluorochrome of Ntziachristos et al., which has an emission wavelength of about 694 nanometers, to teach a fluorescent emission of 694 nanometers. However, at page 18, Ntziachristos et al. describes 694 nanometers to be within a near infrared range, not within a red range as claimed.

With regard to Claims 4 and 24, the Examiner asserts that "Ntziachristos discloses that the fluorescent emission light of the fluorochrome Cy 5.5 is 694nm... ." Furthermore, in his Response to Arguments, the Examiner asserts that "Ntziachristos discloses fluorescent light at 694nm...which falls in the red region of the visible spectrum." Applicants respectfully disagree

and submit that light at 694 nm is in a border region, and is defined by Ntziachristos et al. to be infrared.

Applicants submit that amended Claims 6 and 26 are further patentably distinct over Ntziachristos et al., since the cited reference neither describes nor suggests "... *a tomographic image of the fluorescent proteins*," as set forth in Claims 7 and 28. A described above, Ntziachristos et al. teaches fluorochromes, not fluorescent proteins.

Applicants submit that amended Claims 7 and 28 are further patentably distinct over Ntziachristos et al., since the cited reference neither describes nor suggests "... *the modified diffusion coefficient has the form* $D_\alpha = \frac{1}{3(\mu_s' + \alpha\mu_a)}$, *where* α *is a constant having a value depending on absorption, scattering, and anisotropy of the diffuse medium,* μ_s' *is a reduced scattering coefficient, and* μ_a *is an absorption coefficient*," as set forth in Claims 7 and 28.

In view of the above, Applicants submit that the rejection of Claims 1-7, 9-11, 13, 19-26, 28-30, 32, 38-39, and 44-45 under 35 U.S.C. §102(b) should be removed.

The Rejections under 35 U.S.C. §103(a)

Ntziachristos et al. in View of Takada et al.

The Examiner rejects Claims 8, 12, 14-18, 27, 31, and 33-37 under 35 U.S.C. §103(a) as being unpatentable over Ntziachristos et al. in view of Takada et al. (European Patent Application number 0 336 208).

Claims 8, 12, and 14-18 depend from and thus include the limitations of Claim 1. Thus, Applicants submit that Claims 8, 12, and 14-18 are patentably distinct over the cited references at least for the reasons discussed above in conjunction with Claim 1. Claims 27, 31, and 33-37

depend from and thus include the limitations of Claim 21. Thus, Applicants submit that Claims 27, 31, and 33-37 are patentably distinct over the cited references at least for the reasons discussed above in conjunction with Claim 21.

Applicants submit that Claim 8 is further patentably distinct over Ntziachristos et al., whether taken alone or in combination with Takada et al., since the cited references neither describe nor suggest "... *the light detector is selectively movable to receive the intrinsic light and fluorescent light on a plurality of light paths relative to the specimen*," as set forth in Claim 8.

With regard to Claim 8, the Examiner recognizes that Ntziachristos et al. "...does not disclose expressly selectively movable detector." The Examiner recognizes that Takada et al. teaches "...a selectively movable stage upon which the specimen is located... ." The Examiner asserts that "...[t]he movement between the light source and the specimen versus that of the detector is a matter of apparent motion in different frames of reference." The Examiner asserts that "[i]t would be a simple matter of design choice for one of ordinary skill in the art at the time the invention was made to employ a selectively moveable light source, specimen, detector, or any combination thereof." Applicants respectfully disagree.

According to the Federal Register, Volume 72, No. 195, dated October 10, 2007, at page 57528, Part III of the section entitled "Examination Guidelines for Determining Obviousness under 35 U.S.C. 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.*," an obviousness rejection may be made using the familiar teaching-suggestion-motivation (TSM) rationale... ." In Part III, it is also stated that "[a]lthough the Supreme Court in *KSR* cautioned against an overly rigid application of TSM, it also recognized that TSM is one of a number of valid rationales that could be used to determine obviousness." Thus, as one criteria used to establish prima facie obviousness, there should be some suggestion and motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Applicants

respectfully submit that the Examiner has not shown a suggestion or motivation to modify the references or to combine reference teachings.

In particular, since the references teach only moving the apparent light source and moving the specimen, Applicants submit that one of ordinary skill in the art in possession of Ntziachristos et al. and Takada et al., would not be motivated to move the light paths through the specimen by another means, i.e., by moving the light detector. Applicants submit that the Examiner is merely using hindsight to establish his conclusion of obviousness.

For reasons discussed above in conjunction with Claim 8, Applicants submit that Claim 27 is further patentably distinct over Ntziachristos et al., whether taken alone or in combination with Takada et al., since the cited references neither describe nor suggest "... receiving the intrinsic light and receiving the fluorescent light with *a selectively movable light detector* configured to receive the intrinsic light and fluorescent light on a plurality of light paths relative to the specimen," as set forth in Claim 27.

In view of the above, Applicants submit that the rejection of Claims 8, 12, 14-18, 27, 31, and 33-37 under 35 U.S.C. §103(a) should be removed.

Takada et al. in View of Ntziachristos et al.

The Examiner rejects Claims 40 and 41 under 35 U.S.C. §103(a) as being unpatentable over Takada et al. in view of Ntziachristos et al.

Applicants submit that Claim 40 is patentably distinct over Takada et al., whether taken alone or in combination with Ntziachristos et al., since the cited references neither describe nor suggest "... *at least one selectively movable component to selectively move a projection direction of an apparent light source to direct a plurality of light paths toward a specimen, wherein the selectively movable component includes a selectively movable structure comprising an optical*

fiber, wherein the selectively movable structure is configured to move the optical fiber to a plurality of physical locations to provide the plurality of light paths," as set forth in Claim 40.

With this particular arrangement, an optical fiber serving as a light source can be moved about a specimen.

The Examiner recognizes that Takada et al. teaches a moveable mirror and that Ntziachristos et al. teaches a plurality of fixed in position optical fibers, both to direct light on different paths relative to a specimen being imaged. The Examiner concludes that "[i]t would have been obvious to a person of ordinary skill in the art to employ the optical fibers of Ntziachristos to couple the specimen platform to the detector of Takada." Applicants do not understand the combination proposed by the Examiner and respectfully request clarification.

As an initial matter, Applicants submit that a moveable mirror is not recited in Claim 40, and thus, the combination proposed by the Examiner is not material to the patentability of Claim 40.

Applicants submit that any combination of Ntziachristos et al. and Takada et al. that would achieve the arrangement having the movable optical fiber as an apparent light source as recited in Claim 40 would destroy the intended function of either Ntziachristos et al. or Takada et al.

As found in MPEP §2143.01, in order to establish a prima facie case of obviousness "...[i]f the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims prima facie obvious." (See e.g., In re Ratti, 270 F.2d 810, 123 USPQ 349 (C.C.P.A. 1959)).

Ntziachristos et al. teaches the plurality of optical fibers and Takada et al. teaches a moveable mirror. Providing a movable optical fiber in either Ntziachristos et al. or Takada et al. would completely eliminate the need for the plurality of optical fibers as a light source and for the movable mirror. Thus, providing a movable optical fiber in either Ntziachristos et al. or Takada et al. would entirely change the function of either reference.

In view of the above, Applicants submit that Claim 40 is patentably distinct over Takada et al., whether taken alone or in combination with Ntziachristos et al.

Claim 41 depends from and thus includes the limitations of Claim 40. Thus, Applicants submit that Claim 41 is patentably distinct over the cited references at least for the reasons discussed above in conjunction with Claim 41.

In view of the above, Applicants submit that the rejection of Claims 40 and 41 under 35 U.S.C. §103(a) should be removed.

Claims 50 and 51 are new in the application. Consideration of new Claims 50 and 51 is respectfully requested. Support for new Claims 50 and 51 can be found, for example, at paragraph [0044] of the published US application, which is recited above.

In view of the above Amendment and Remarks, Applicants submit that the claims and the entire case are in condition for allowance and should be sent to issue and such action is respectfully requested.

The Examiner is respectfully invited to telephone the undersigning attorney if there are any questions regarding this Amendment or this application.

The Assistant Commissioner is hereby authorized to charge payment of any additional fees associated with this communication or credit any overpayment to Deposit Account No. 500845, including but not limited to, any charges for extensions of time under 37 C.F.R. §1.136.

Respectfully submitted,

Dated: Oct 14, 2009

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Attachment: first page at web site http://en.wikipedia.org/wiki/Light .

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Light

From Wikipedia, the free encyclopedia

Light is electromagnetic radiation, particularly radiation of a wavelength that is visible to the human eye (about 400–700 nm, or perhaps 380–750 nm[1]). In physics, the term *light* sometimes refers to electromagnetic radiation of any wavelength, whether visible or not.[2][3]

A beam of white light (entering upwards from the right) is dispersed into its constituent colors by its passage through a prism. The fainter beam of white light exiting to the upper right has been reflected (without dispersion) off the first surface of the prism.

Four primary properties of light are:

- Intensity
- Frequency or wavelength
- Polarization
- Phase

Light, which exists in tiny "packets" called photons, exhibits properties of both waves and particles. This property is referred to as the wave–particle duality. The study of light, known as optics, is an important research area in modern physics.

Contents

Speed of light